82

WHAT IS CLAIMED IS:

1. An oligomeric compound comprising at least one monomeric sub-unit of structure I:

$$Q_1$$
 Q_2
 Z

Structure I

wherein:

5 X is hydroxyl or amino;

R is halo or C_1 - C_6 alkyl or substituted C_1 - C_6 alkyl wherein said substitution is halo, amino, hydroxyl, thiol, ether or thioether;

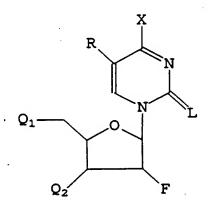
L is oxygen or sulfur;

In the second 2 is fluoro or $O-R_1X_1$, where R_1 is C_1-C_6 alkyl, C_6-C_{10} aryl, C_7-C_{18} alkaryl and X_1 is H, NH_2 or imidazole; and

one of Q_1 and Q_2 is attached via a linking moi ty to a nucleotide, oligonucleotide, nucleoside, or oligonucleoside and the other of said Q_1 and Q_2 , is a hydroxyl, a

- 15 protected hydroxyl, an activated solid support, a nucleotide, an oligonucleotide, a nucleoside, an oligonucleoside, an oligo-nucleotide/nucleoside, an activated phosphate, a phosphate, an activated phosphite, or a phosphite.
- The oligomeric compound of claim 1, wherein L
 is O.
 - 3. The oligomeric compound of claim 1, wherein ${\tt Z}$ is ${\tt F}.$

- 4. The oligomeric compound of claim 1, comprising from 5 to 200 sub-units.
- 5. The oligomeric compound of claim 1, comprising from 5 to 50 sub-units.
- 5 6. The oligomeric compound of claim 1, comprising from 10 to 20 sub-units.
- The oligomeric compound of claim 1, wher in said linking moiety comprises a phosphodiester, phosphotriester, hydrogen phosphonate, alkylphosphonate,
 alkylphosphonothicate, arylphosphonothicate, phosphorothicate, phosphorodithicate, or phosphoramidate.
 - 8. The oligomeric compound of claim 1 having a plurality of monomeric sub-units of structure I.
- The oligomeric compound of claim 8 wherein
 said monomeric sub-units are located at preselected positions.
 - 10. An oligomeric compound comprising at least one monomeric sub-unit of structure II:



Structure II

wherein:

X is hydroxyl or amino;

R is halo or C_1 - C_6 alkyl or substituted C_1 - C_6 alkyl wherein said substitution is halo, amino, hydroxyl, thiol, 5 ether or thioether;

L is oxygen or sulfur; and

one of Q_1 and Q_2 is attached via a linking moiety to a nucleotide, oligonucleotide, nucleoside, or oligonucleoside and the other of said Q_1 and Q_2 , is a hydroxyl, a protected hydroxyl, an activated solid support, a nucleotide, an oligonucleotide, a nucleoside, an oligonucleoside, an oligonucleotide/nucleoside, an activated phosphate, a phosphate, an activated phosphite, or a phosphite.

- 15 11. The oligomeric compound of claim 10, wherein L is O.
 - 12. The oligomeric compound of claim 10, comprising from 5 to 50 sub-units.
- 13. The oligomeric compound of claim 10,20 comprising from 10 to 20 sub-units.

- 14. The oligomeric compound of claim 10, wherein said linking moiety comprises a phosphodiester, phosphotri ster, hydrogen phosphonate, alkylphosphonate, alkylphosphonothicate, arylphosphonothicate,
 5 phosphorothicate, phosphorodithicate, or phosphoramidate.
 - 15. The oligomeric compound of claim 10 having a plurality of monomeric sub-units of structure II.
- 16. The oligomeric compound of claim 15 wherein said monomeric sub-units are located at preselected10 positions.
 - 17. An oligomeric compound comprising at least one monomeric sub-unit of structure III:

$$Q_1$$
 Q_2
 Q_2
 Q_1
 Q_2
 Q_2
 Q_1
 Q_2
 Q_2
 Q_3
 Q_4
 Q_4
 Q_5
 Q_5
 Q_7
 Q_8

Structure III

wherein:

X is hydroxyl or amino;

R is halo or C_1 - C_6 alkyl or substituted C_1 - C_6 alkyl wherein said substitution is halo, amino, hydroxyl, thiol, ether or thioether;

L is oxygen or sulfur;

 $$R_1$$ is $C_1\text{--}C_6$ alkyl, $C_6\text{--}C_{10}$ aryl, $C_7\text{--}C_{18}$ alkaryl and X_1 20 is H, NH_2 or imidazole; and

one of \mathbb{Q}_1 and \mathbb{Q}_2 is attached via a linking moiety to a nucleotide, oligonucleotide, nucleoside, or oligonucleo-

sid and the other of said Q₁ and Q₂, is a hydroxyl, a pr tect d hydroxyl, an activated solid support, a nucleotide, an oligonucleotide, a nucleoside, an oligonucleoside, an oligo-nucleotide/ nucleoside, an activated phosphate, a phosphate, an activated phosphite, or a phosphite.

- 18. The oligomeric compound of claim 17, wher in L is O.
- 19. The oligomeric compound of claim 17,10 comprising from 5 to 50 sub-units.
 - 20. The oligomeric compound of claim 17, comprising from 5 to 50 sub-units.
- 21. The oligomeric compound of claim 17, wherein said linking moiety comprises a phosphodiester,15 phosphotriester, hydrogen phosphonate, alkylphosphonate, alkylphosphonothioate, arylphosphonothioate, phosphorodithioate, or phosphoramidate.
 - 22. The oligomeric compound of claim 17 having a plurality of monomeric sub-units of structure I.
- 23. The oligomeric compound of claim 22 wherein said monomeric sub-units are located at preselected positions.
 - 24. A process for the synthesis of a 2'-O-substituted pyrimidine nucleoside of formula:

$$R^2-O$$
 O O O

wherein:

Q is a

pyrimidine base or a 2-S pyrimidine base;

R¹ is substituted or unsubstituted C₁-C₃₀ alkyl, C₁-5 C₃₀ alkenyl, C₁-C₃₀ alkynyl, C₆-C₁₄ aryl, or C₇-C₃₀ aralkyl, wherein said substitution is halo, amino, hydroxyl, thiol, ether or thioether; and

 ${\ensuremath{R^2}}$ and ${\ensuremath{R^3}}$ are independently hydrogen or a hydroxyl protecting group;

10 comprising the steps of:

providing a 2-2'-anhydropyrimidine nucleosid; selecting an alcohol of the formula R¹-OH; and treating said 2-2'-anhydropyrimidine nucleoside and said alcohol with a Lewis acid under conditions of time, temperature and pressure effective to yield said 2'-O-substituted pyrimidine nucleoside.

- 25. The process of claim 24 wherein said 2-2'-anhydropyrimidine nucleoside and said alcohol are treated in a pressure sealed vessel.
- 26. The process of claim 24 wherein said Lewis acid is a borate.
 - 27. The process of claim 26 wherein said borate is a trialkyl borate.
- 28. The process of claim 27 wherein the formula of 25 said trialkyl borate is $B(OR^1)_3$.
 - 29. The process of claim 28 wherein said trialkyl borate is prepared from the treatment of borane with an

alcohol.

30. The process of claim 29 wherein said trialkyl borate is prepared from the treatment of boran with an alcohol of formula $HO-R^1$.

- 5 31. The process of claim 24 wherein R^1 is $C_1 C_{10}$ alkyl.
 - 32. The process of claim 24 wherein R^1 is $C_6 C_{14}$ aryl.
- 33. The process of claim 24 wherein said treating 10 comprises heating at from about 120 $^{\circ}\text{C}$ to about 200 $^{\circ}\text{C}$.
 - 34. The process of claim 24 wherein said pyrimidine nucleoside is uridine or 5-methyluridine.
 - 35. A process for the synthesis of a 2'-0-substituted cytidine nucleoside of formula:

15 wherein:

X' is O or S;

 R^1 is substituted or unsubstituted C_1 - C_{30} alkyl, C_1 - C_{30} alkenyl, C_1 - C_{30} alkynyl, C_6 - C_{14} aryl, or C_7 - C_{30} aralkyl, wherein said substitution is halo, amino, hydroxyl, thiol, 20 ether or thioether;

 \mathbb{R}^2 and \mathbb{R}^3 are independently hydrogen or a hydroxyl protecting group;

PCT/US96/03174

R⁵ and R⁶ ar independently H, C₁-C₃₀ hydrocarbyl or substituted C₁-C₃₀ hydrocarbyl; comprising th steps of:

. 89

providing a 2-2'-anhydrouridine nucleoside of 5 formula:

selecting an alcohol of formula R1-OH; treating said 2-2'-anhydrouridine nucleoside and said alcohol with a Lewis acid under conditions of time, temperature and pressure effective to form a 2'-0-10 substituted uridine nucleoside; and

aminating said 2'-O-substituted uridine nucleoside to said 2'-O-substituted cytidine nucleoside.

- The process of claim 35 wherein said 2-2'anhydrouridine nucleoside and said alcohol are treated in a 15 pressure sealed vessel.
 - The process of claim 35 wherein said Lewis acid is a borate.
 - The process of claim 37 wherein said borate is a trialkyl borate.
- 20 The process of claim 38 wherein the formula of said trialkyl borate is B(OR1)3.
 - The process of claim 38 wherein said trialkyl borate is prepared from the treatment of borane with an

alcohol.

41. The process of claim 40 wherein said trialkyl borate is prepared from the treatment of borane with an alcohol of formula $HO-R^1$.

- 5 42. The process of claim 35 wherein R^1 is $C_1 C_{10}$ alkyl.
 - 43. The process of claim 35 wherein R^1 is $C_6 C_{14}$ aryl.
- 44. The process of claim 35 wherein said treating 10 comprises heating from about 120 °C to about 200 °C.
 - 45. The process of claim 35 wherein said 2'-0-substituted cytidine nucleoside is 2'-0-methyl-5-methylcytidine.
- 46. An oligomeric compound comprising at least one 15 monomeric sub-unit of formula:

$$Q_1$$
 Q_2
 Q_2
 Q_3
 Q_4
 Q_5
 Q_7
 Q_7
 Q_7

wherein:

A is hydroxyl or amino;

R is halo or C_1 - C_6 alkyl or substituted C_1 - C_6 alkyl wherein said substitution is halo, amino, hydroxyl, thiol, 20 ether or thioether;

- L is oxygen or sulfur;
- Z' is substituted or unsubstituted C_1-C_{30} alkyl, C_1-C_{30} alkenyl, C_1-C_{30} alkynyl, C_6-C_{14} aryl, or C_7-C_{30} aralkyl, wherein said substitution is halo, amino, hydroxyl, thiol, 5 ether or thioether; and

one of Q₁ and Q₂ is attached via a linking moiety to a nucleotide, oligonucleotide, nucleoside, or oligonucleoside and the other of said Q₁ and Q₂, is a hydroxyl, a protected hydroxyl, an activated solid support, a nucleotide, an oligonucleotide, a nucleoside, an oligonucleoside, an oligo-nucleotide/nucleoside, an activated phosphate, a phosphate, an activated phosphite, or a phosphite.

- 47. The oligomeric compound of claim 46, wherein L 15 is O.
 - 48. The oligomeric compound of claim 46, wherein Z is $-(CH_2)_n-O-(CH_2)_n-CH_3$.
 - 49. The oligomeric compound of claim 48, wherein nois 2 and m is 0.
- 20 50. The oligomeric compound of claim 46, comprising from 5 to 200 sub-units.
 - 51. The oligomeric compound of claim 46, comprising from 5 to 50 sub-units.
- 52. The oligomeric compound of claim 46, 25 comprising from 10 to 20 sub-units.
- 53. The oligomeric compound of claim 46, wherein said linking moiety comprises a phosphodiester, phosphotriester, hydrogen phosphonate, alkylphosphonate, alkylphosphonothioate, arylphosphonothioate, phosphorothioate, phosphorothioate, phosphoro-30 dithioate, or phosphoramidate.

- 54. The oligomeric compound of claim 46 having a plurality of monomeric sub-units of said formula.
- 55. The oligomeric compound of claim 54 wherein said monomeric sub-units are located at preselected 5 positions.